MELANCHOLIA WITH DELUSIONS OF NEGATION: THREE CASES WITH AUTOPSY[1]

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While engaged upon a more general analysis of involution-melancholia, presenile insanity, and allied conditions, our attention was arrested by three cases of melancholia showing feelings of unreality. Recent interest has been so great in patients with feelings of unreality and nihilistic delusions that we have been tempted to anticipate our more general report upon the great subsenile group with a particular account of these three cases. The cases present a certain uniformity both from a clinical point of view and from the histopathological side. Anatomically, the cases belong in the catalogue of insane subjects with "normal" brains or brains with "unimportant" or "trifling" lesions. It is these cases which now deserve the closest histopathological attention, especially from the point of view of the intracellular pigments and fats and their distribution. The problem in these cases of "normal" brains might shift from considering foci of destruction to determining the degrees and loci of intracellular clogging with pigments and fats.

The paper deals with three cases of melancholia which showed feelings of unreality and nihilistic delusions, but is not to be taken as a brief for Cotard's syndrome as an entity among mental diseases. Nevertheless, feelings of unreality and nihilistic delusions, together with various other ideas of a metaphysical cast, are so striking an element in certain conditions of melancholia that we can hardly escape throwing such cases into a group for convenience at least. Moreover, although delusions of this type undeniably dwell in the minds of many persons in and about the climacteric era and although the climacteric state appears to have many features which are met again and again and afford some color to the claim of melancholia as an entity, we do not wish at present to concede that either Cotard's syndrome or melancholia at large is an ultimate group for a finished psychiatry.[2]

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[1] From the wards and laboratory of the Danvers Insane Hospital. The term melancholia is here used in the older Kraepelinian sense.

Histopathology can have little to say on the cerebral side so long as the metabolism of involution presents such meager data. The present cases, however, so far as their examination was carried, offer interesting data which support the claim of a central rather than a peripheral disorder as the basis for the mental states shown. Moreover, the central disorder appears to involve, not so much the great cells which are related to the periphery, as the smaller cells which must be concerned with the elaboration and transforming of peripheral data.

Should our hypothesis hold, the cases of so-called melancholia (including many of those which fall into Cotard's syndrome) might prove to be founded on a central disease. The importance cannot be denied of proving that these patients are not simply explaining and rationalizing their own perverted metabolism, but are actually suffering from a fault in the very mechanism of explanation and rationalizing. Naturally the cerebral fault may itself turn out to be metabolic. We can have nothing to say on this line and offer our cases as preliminary to a more extensive study of the group called melancholia.

CASE I.—G. E. H. Admitted to Danvers Insane Hospital July 10, 1903. Age, 49. Occupation, clerk.

Family History.—His father was an eccentric, incapable man, and there was a history of occurrence of insanity in distant relatives on paternal side. The relationship and character of mental disturbance could not be ascertained.

Personal History.—Naturally, he was a man of cheerful, pleasant temperament, with average business capacity. His habits in regard to alcohol were good. There was no history or evidence of syphilis. Previous to present illness he had had lumbago on several occasions, but no well-defined attacks of rheumatism or any other disorder which could account for the cardiac hypertrophy found on admission. The occurrence of previous mental disturbance was denied by relatives. During the winter of 1902–1903, he lost money, became depressed, slept poorly, lost weight and had to give up work in February, 1903. His depression deepened and he became restless and agitated, fancied that he was ruined and in a hopeless condition.

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[2] Since this paper was first presented, Dreyfus has published "Die Melancholie ein Zustandsbild des manisch-depressiven Irreseins," 1907, representing a reversal of Kraepelinian opinions concerning melancholia as an entity.

He was admitted to the McLean Hospital, April 28, 1903. We are indebted to Dr. Tuttle for clinical notes which have been used in the case description. Upon admission at Danvers examination was made by Dr. H. M. Swift.

Physical Condition.—July 11, 1903. His muscular development was good, but he was poorly nourished. Area of cardiac dullness was enlarged to the left, and apex beat was in sixth space. There was a systolic murmur heard most plainly at the apex and transmitted to the axilla. Pulse was 90–100, increased tension, and radials were somewhat thickened. Urinary examination was negative. Cranial nerves were normal. Pupils equal and reacted to light. Tendon reflexes were lively and equal. No disturbance of sensation was found.

The notes on the mental condition from April 28 to July, 1903, are as follows: During the month of May there were short periods when orientation for time and place was imperfect, and at these times he had imperfect memory and displayed great agitation. He was distinctly apprehensive, thinking the register was a machine to kill him; that he had signed away the whole United States; that he had opened all the asylums in the United States; that he had killed his wife and could see her blood on his hands. At times, he appreciated the absurdity of these ideas and would converse clearly. Gradually his apprehensiveness and agitation increased, though at intervals he would demonstrate a good grasp upon surroundings. He became resistive, talked in anxious whispered tones between moans and sighs, and developed the feeling of unreality, seated, rocking body to and fro, wringing his hands; he would whisper between his groans and sighs: "I am all mixed up. It's all a mistake. I'm not Mr. H——. I am all gone, I am dead to the world." Again he would say: "I'm not G. E. H., I ought to be him, but I've taken these names along when I have seen them in the yard. I've made myself as Gibbs, I've been here as G. E. H., and have a home in Haverhill; not I, but G. E. H., has a home in Haverhill. I've made myself a different one."

His agitation increased, and he became untidy and very resistive. His productions became desultory and disconnected. He denied identity, had no stomach, could not take food, and at the last had no idea of time or place. He died of pneumonia July 13, 1903.

Summary of Case I.—Father was eccentric and there were instances of insanity on paternal side of family. Age, 49. Habits exemplary. Loss of money only recognizable cause for gradually increasing worry and depression. No serious illness previously. Cardiac hypertrophy, arterio-sclerosis, only recognized physical ailments.

Mental symptoms appeared in following order: worry, insomnia, restlessness, depression, delusions, possibly visual hallucinations, agitation, ideas of negation and stuporous condition preceding death. Orientation fairly well preserved until the last few days.

Autopsy Findings.—The autopsy was performed by Dr. A. M. Barrett and showed death due to pneumonia of the right lower lobe, lower portion of upper lobe, and posterior portion of the middle lobe of left lung. The heart muscle was pale and flabby. The mitral valve was moderately thickened. There were a few patches of atheroma in thoracic portion of the aorta. The liver showed slight surplus of fat. The heart weighed 445 grams. There was a chronic fibrous peritonitis in the region of the appendix and upon the lower surface of the liver and around the gall-bladder. Examination of the skull showed the sutures preserved and the diploë in large amount. The dura mater firmly adherent to the calvarium. The brain with pia mater weighed 1445 grams. The pia mater contained considerable fluid and was hazy along the edge of vessels. Adhesions were found at the bottom of the fissures of Sylvius. The large blood vessels at the base showed some yellow atheromatous patches of irregular distribution. The lumina of the arteries were not diminished. The choroid plexuses showed a few minute cysts. There were no focal areas of softening in the brain. The ependyma of the ventricles was smooth.

Microscopical Examination.—Several regions of the cerebral cortex in both hemispheres showed an essentially normal layering (Nissl's method). There are nowhere focal destructive lesions. One lesion is common to all the sections examined, viz., a great quantity of pigmented cells in the adventitiæ of the vessels in all parts of the gray and white matter (best demonstrated in Heidenhain iron hematoxylin preparations). The pigment around the larger vessels is enclosed in cells of the usual meningeal phagocyte type. But about the capillaries of the gray matter the pigment is as a rule enclosed in neuroglia cells.

The source of the perivascular pigmentation cannot be made out from the vessels affected, since all the vessels with but few exceptions are equally invested with pigmented cells. The distribution of pigment in neuroglia cells is a little more characteristic. The pigmentation of neuroglia cells is not, as in some conditions, particularly found in the outer or subpial layer or in the inner or fusiform cell layer. The neuroglia cell pigmentation tends to affect the intermediate layers of the cortex. This is best shown in the layers of large and small stellate cells of the calcarine areas. The frontal areas, however, show a fairly general distribution of pigmented neuroglia cells.

The nerve cell pigmentations are more characteristic in point of distribution. The large pyramidal cells of the frontal cortex are practically all pigmented and, in most cases, somewhat characteristically along the lateral borders and at the inferior angles, leaving the perinuclear region and the apical portion free of pigment. The pigment is not collected in a single sac, but appears to occupy interstices of the cells with perfect maintenance of their proper contours. The characteristic unifocal collections of pigment in the Betz cells of the paracentral lobules are absent in this case. The Betz cells have little or no pigment of any sort. The larger nerve cells (including the solitary cells of Meynert) of the calcarine areas fail to show much pigment.

The examination indicates a steady outward stream of pigment materials from the nerve tissues to the perivascular region. So far as the examination of a limited number of areas is conclusive, the autochthonous pigmentation of the nerve cells is maximal in cell types whose function is either unknown or receptive. Large elements like the Betz cells and the solitary cells of Meynert fail to show marked pigmentation. These larger elements are doubtless more directly related with the projection system than the others.

Case II.—T. H. Admitted to Danvers Insane Hospital June 13, 1904. Age, 75. Occupation, mason.

Family History.—Both maternal and paternal relatives were unusually healthy, long-lived people. His mother died at the age of 63, and had exhibited a continuous, melancholy depression for the last few years of life. One brother died of apoplexy at the age of 52. Family history was otherwise negative.

Personal History.—He had a normal development and became a capable and modestly successful contractor, retiring from business at the age of 65, with a small competency. His temperament was cheerful and sociable. Family relations were pleasant. At no period of life had he ever used distilled liquors, but occasionally he drank a little beer with meals.

At the age of 25, he had a venereal lesion, probably nonspecific. Aside from an attack of pneumonia seven years prior to commitment, he had always been healthy. His relatives had noted some memory failure for recent events during a few years before admission, and he had been troubled with insomnia for one year, but no symptoms of insanity were recognized until the week before his commitment. The loss of an only son eight years before, who left a widow and four children dependent upon the patient for support, had been the only known cause for worry. A sudden depression developed. He thought he had lost all his property and that he was responsible for the consequent misery of his family. He became sleepless for a week and finally cut his throat, wounding the larynx. He struggled to prevent dressing of the wound, declaring that he did not want attention, that he must die; and threatened to accomplish suicide by some other means. He was soon admitted to the hospital.

Physical Condition.—He had a powerful muscular development, was well nourished, tissues showing very little senile atrophy. There was an infected wound involving larynx. Temperature on admission 99.4°. There was harsh respiration and occasional coarse rales were heard over anterior surface of chest. Area of cardiac dulness slightly enlarged. Second aortic sound was sharp and accented. First sound at apex was roughened. Pulse was 126, fair tension, irregular rhythm and occasionally intermittent. Superficial arteries were thickened and tortuous, and there was well-defined arcus sensilis. Urine showed trace of albumin. No sugar. Sediment contained hyaline casts, pus cells, uric acid and calcium oxalate crystals. Strength was little impaired and he had perfect control of muscular movements.

Cranial nerves were normal. Pupils were responsive to light. Tendon and skin reflexes were normal. No sensory disturbance detected.

Mental Condition.—At time of admission, he was oriented for time, place and persons, and appreciated the character of his surroundings, but answers had to be obtained between his groans and protestations. His mental distress and agitation rapidly became more pronounced, and he would pace about his room, wringing his hands, his features contorted with emotion, muttering about his "most miserable state," his family and his deplorable acts. With great and steadily increasing difficulty his attention could be gained momentarily, but most of the time he took little notice of requests and struggled blindly against efforts to care for him. His spontaneous talk showed great depression, nihilistic delusions with the feeling of unreality; *e. g.*, "Oh! I am in a hopeless state. It is awful and nobody ever suffered this way. This is not a reality. This is eternity, this is eternity. Why such a thing as I the world never knew, the world never saw. Why! Why! Why! I can't move, I can't die." As nourishment was offered he said: "No, no, I can't take it. It won't do me any good. I can't take it, I am not a reality." At another time, he declared he was in a vault, and that the sunlight, streaming into the room was not real; that the sky was not blue; that the view from his window was not a reality; that the people about him were not real human beings, and that no person had ever been in such a miserable state as himself. His agitation was practically continuous. He would appear exhausted and lie down and secure short, fitful sleep. The suppurating laryngeal wound eventually, prevented audible speech, and death resulted from pneumonia on the eighth day in hospital.

Summary of Case II.—Mother had mental depression during last four years of life. Brother apoplectic. Age, 75. Moderate beer drinker. Old age and worry over loss of son and responsibility of caring for son's family only known causes for a comparatively sudden outbreak. No known illness, excepting pneumonia, seven years previously. Arteriosclerosis, nephritis, myocarditis and bronchitis from wound in larynx were the only physical ailments noted. Slight memory failure and some insomnia preceded for some months a sudden depression, painful delusions concerning self and family, suicidal attempt, great motor agitation, feelings of unreality largely confined to external objects, and nihilistic ideas. Orientation fairly preserved to the last few days of life.

Autopsy Findings.—The autopsy was performed by Dr. A. M. Barrett and showed death probably due to hypostatic pneumonia. Suicidal wound of neck. The heart was fatty. Arteriosclerosis was general, involving the aorta and in particular the splenic vessels and the arteries of the base of the brain. There was well-marked chronic diffuse nephritis. Examination of the head showed the following: dura mater completely and firmly adherent to the calvarium. The pia mater free from thickening. Basal arteries beset with scattered foci of yellow thickening. Internal carotid arteries notably stiff and yellow. Small old cyst of softening just outside tip of posterior horn of right lateral ventricle. The brain with pia mater weighed 1,300 grams.

Microscopical Examination.—The frontal, paracentral and calcarine regions of the cerebral cortex show essentially normal layering. The most prominent feature is a universal pigmentation of perivascular cells, neuroglia cells, and nerve cells of about the same degree in all regions examined. The pigmentation about the vessels is by no means maximal, and is of a degree often shown in younger subjects under different conditions. The neuroglia cell pigmentation affects practically all the cells and, since it occurs also in the subpial layer, is probably due to fiber degeneration as well as to nerve cell changes. Satellite cell pigmentation is, however, also frequent and characteristic, so that a nerve cell origin for some of the pigment is highly probable. The examination of the nerve cell pigmentation is facilitated by parallel study of adjacent sections stained by Nissl's methylene blue method and by Heidenhain's iron hematoxylin method. By Nissl's method it is easy to make out the universality and extent of the senile yellow pigmentation in the layer elments, *e. g.*, large pyramidal cells, Betz cells, solitary cells of Meynert. Besides the yellow pigmentation of the banal type shown in old age, the Heidenhain preparations show an extensive development of pigment staining black by this method. This latter black-stained pigment lodges in the nerve cells of the intermediate layers, but characteristically affects the smaller elements, *e. g.*, small pyramidal cells, as well as also the large pyramidal cells (in which the black-stained pigment accompanies the yellow pigment which remains unstained). The Betz cells and the solitary cells of Meynert, despite their accumulations of or distention with yellow pigment, fail to show more than a very few black globules in the Heidenhain preparations. The black-staining pigment seems never to alter the cell form, but to lie in crevices which may represent lost tissue. The Nissl stain shows that the Nissl bodies are throughout not well stainable; but this circumstance cannot yet be unequivocally related to the cell pigmentation.

The arteriosclerotic element in this case is not prominent, despite the old cyst of softening in the left occipital region. Nor is cerebral atrophy a prominent feature. The most striking features are extensive pigmentations, which are partly of senile origin and partly reside in elements which are of unknown or receptive function. These two types of pigmentation are easily separable in the Heidenhain preparations.

CASE III.—J. H. A. Admitted to Danvers Insane Hospital, November 21, 1903. Age, 65. Occupation, shoemaker.

Family History.—Patient's father died of some cardiac disorder at age of 77. His mother died at the age of 67, after suffering from senile dementia for over three years. One brother died of tuberculosis. The history concerning grandparents and collateral branches was unobtainable.

Personal History.—Nothing was known of early life. He enlisted in the army, serving three years during the Civil War, and was afterwards employed as a shoe-factory operative. He was married in 1873, and has two healthy adult children. His wife stated that he had been industrious, kind to family, pleasant and agreeable in disposition. Since early life he had been a moderate user of tobacco and alcohol. He was not a daily drinker and was never known to have been intoxicated.

He had had a purulent discharge from the right ear following scarlet fever at the age of three. This was the only severe illness he had had until the age of 61, when he had typhoid fever and la grippe during the same year and was mildly delirious during both illnesses. He made good recoveries and worked steadily until nine weeks before his commitment, when he was discharged for failure to perform work properly. For two or three months previous to this event he had slept poorly, lost weight, worried over trifles, and had shown evidences of mild hypochondriacal depression. Following the loss of his position, mental symptoms had been progressive. He began to think that he and his family would starve and freeze, and was greatly distressed by fancied physical ailments; *e. g.*, he had the idea at one time that his head, eyes and limbs were growing large and later thought that he had become much smaller than others who were correspondingly increased in size. Occasionally he would seem to have some insight, and he lost weight steadily. He never showed any suicidal tendencies. A sudden threat of violence to members of his family and refusal of food were the immediate causes of his hospital commitment.

Physical Condition.—He had slender muscular development, pallid complexion and was poorly nourished. His skin was dry and wrinkled. He had sordes on lips and teeth, tongue was coated and breath foul. Temperature ranged from 99° to 100°. Area of cardiac dulness was not increased. Second aortic sound was sharp and accented, and first sound at apex was roughened. Pulse was 96, feeble volume and irregular rhythm. Arteries were soft. There was a faint arcus senilis.

Abdomen was shrunken. Urine was turbid and had a foul odor. Acid. Sp. gr. 1013. No sugar or albumin present. Sediment showed squamous epithelial cells, few red corpuscles, bacteria and moulds. He had accurate control of muscular movements, and walked with a firm gait. He could hear faint watch tick with left ear and could read coarse print. The right pupil was slightly larger than left, and both reacted promptly to light. Tendon reflexes were generally hyperactive and equal. Sensory tests were of little value, as he declared that he had no feeling, although wincing at pin pricks.

Mental Condition.—Soon after admission, he objected to every effort to care for him. He refused to walk, said that he had no legs and could not stand; when an attempt was made to raise him from a sitting position he doubled up his limbs and shouted protests against the cruelty of trying to make a man with no legs walk. His enunciation was not impaired and he talked freely, excepting that he would refuse to answer some questions and remain mute for a short time. In answering questions to test orientation, grasp on surroundings and retention of school knowledge, he would give correct replies after protests, refusals, and nihilistic statements; *e. g.*, Q. Where are you? A. "I don't know, I've got no brains. Yes I do too, Danvers. I've been here. Down here for insane and you are going to report I am all right." Q. Are you sick? A. "Course I am, and you know it. I've got no brains and I can't talk and you are going to make out the wrong report. I've got no heart and no stomach, and I can't swallow. I haven't any feelings." His tones were sharp and manner petulant. He was apprehensive and showed some agitation. There was no evidence of retardation. After much urging he would swallow liquid nourishment in great quantities, but saying it did him no good, because he had no stomach, nothing but a hole and he would drink to fill that up. Every question would suggest some new idea. When asked if he knew any people about him, he answered: "Yes, you are all great big men and so strong, you must weigh over 400 pounds, and I'm so small you can't see me. I'm freezing to death and you cover me up with great, heavy, wet blankets. I wouldn't burn if you threw me in the hottest furnace, but I can't suffer because I've got no brains."

He would say that he could remember nothing of events from day to day because he had "no brains" and in the same sentence make remarks that showed partial recollection. Depression was constant and at times was very marked. During the first week in hospital he was restless, walking to and fro in his room, groaning and picking at his clothing and fumbling with his bedding. He was occasionally untidy in habits. With increasing weakness, his ideas of negation and unreality became more absurd, and were more brokenly expressed. Death occurred December 19, 1903.

Summary of Case III.—Mother died of senile dementia at 67. Moderate use of alcohol. Age, 65. No assignable cause for insanity. Typhoid and la grippe with delirium accompanying both disorders, four years previously.

Emaciation, arteriosclerosis of mild degree, nephritis, cystitis and lively reflexes were the only important physical ailments. Mental symptoms gradual in onset. Slowly increasing hypochondriacal depression, with incapacity for work, was noted for four months before evolution of ideas of unreality and nihilistic delusions. Mildly agitated, petulant and complaining during the last. Orientation and memory quite well preserved.

Autopsy Findings.—The autopsy was performed by Dr. A. M. Barrett, and showed an extensive suppurative process in the retroperitoneal tissue around the bladder with abscesses anterior to the bladder and numerous narrow sinuous pus channels running backward on either side of the bladder. The process extended upward beyond the limits of the pelvis into the perinephritic fat tissue as far as the upper poles of the kidney.

The right auricle of the heart showed numerous small thrombi. There were numerous recent emboli in the primary branches of the left pulmonary artery. The aorta showed, 30 cm. below the arch, a large thrombus with puriform softening. The spleen had failed to react to septicemia. The lungs, pancreas, renal pelves, ureters and bladder showed various signs of acute inflammation. Moderate aortic sclerosis. The brain showed no gross signs of alteration at the autopsy and was hardened for four weeks in ten per cent. formaldehyde solution. More careful examination later also proved negative. The ependyma of ventricles was smooth.

Microscopical Examination.—Cultures from the heart's blood and retroperitoneal pus showed pneumococcus and a bacillus, probably bacillus coli communis. Examination of the organs of the trunk added little to the gross findings. The kidneys showed a mild chronic interstitial change with slight fatty changes in the epithelial lining of the tubules.

Microscopical examination of the various regions of the cerebral cortex by Nissl's method, by L. Ehrlich's pyronin method for plasma cells, and by Heidenhain's iron hematoxylin method demonstrated a moderate and in places quite trivial accumulation of cells of the lymphocyte group in the sheaths of small vessels in the lower layers of the gray matter and the adjacent white matter. This accumulation of lymphocytes (and plasma cells) is strikingly even in degree in the parts examined (left and right superior frontal, left and right paracentral, left and right calcarine and occipital regions) and in most sections has to be sought with some care. There is no noteworthy alteration of the nerve-cells, if we except pigmentation of the larger elements (large pyramidal cells of frontal area, Betz cells, large pyramidal cells of occipital area). The other nerve elements (in particular the solitary cells of Meynert) fail to show pigmentation. Numerous neuroglia cells, as well as cells applied to the walls of capillaries, are well pigmented (seen especially in the Heidenhain preparations). The cell layers of the cortex and the cell arrangements of the white matter show no notable alteration.

The question arises whether the data admit the diagnosis *general paresis*. A strict histological diagnosis might be chronic degenerative and exudative encephalitis of a diffuse but mild nature with the exudative element slightly predominant.

SUMMARY OF POST-MORTEM FINDINGS.

The causes of death were: Case I, pneumonia; Case II, pneumonia following suicidal wound of neck; Case III, general infection from pelvic suppuration.

All three cases presented more or less sclerosis of the aorta. The senile case (II) and case I showed considerable sclerosis of the large arteries of the base of the brain.

Aside from a small old cyst of softening in case II, no brain showed focal destructive lesions. No brain gave sign of general or focal atrophy upon macroscopic examination. Case I was the only case to show pia mater changes, and these were confined to haziness along vessels and adhesions at the bottoms of the Sylvian fissures. Case III, despite the chronic exudate found upon microscopic examination, showed no macroscopic alterations of the pia mater. The ependyma was in all cases smooth.

Microscopical examination of three or more areas in each hemisphere was carried out by several methods, notably by Nissl's original methylene blue method and by Heidenhain's iron hematoxylin method.

Common to all the cases is an accumulation of meningeal *phagocytes containing pigment.* This perivascular pigmentation is of about the same degree and quality as that found in most adults beyond the age of fifty years. Whether perivascular cell pigmentation signifies increased wear and tear on the part of the nervous tissues, or whether it rather signifies a reduction in the serum's power to take up these substances cannot yet be told with assurance.

A second common feature of the cases is *neuroglia cell pigmentation.* Whether the collections of pigment (or of fat-like bodies) here shown indicate phagocytosis on the part of these cells cannot be established. The accumulations of fat-like substances might be due to some neuroglia cell activity affecting materials brought to the cells in solution. The senile case showed well-marked satellite-cell pigmentation. The neuroglia-cell pigmentation which is found common to all three cases is pigmentation of the scattered neuroglia cells of the middle layers of the cortex.

The nerve cells also show deposits of pigment or fat-like substances. The Heidenhain preparations bring out the presence of two kinds of pigment, which can be distinguished according to capacity or lack of capacity to take up the hematoxylin. The type of pigment which fails to take up hematoxylin is collected in the familiar yellow sacks which form unifocal deposits in the cytoplasm of the larger cells. This yellow pigmentation is found in case II, as it is in numerous senile and subsenile conditions. It is this pigment which is so common that histologists attach little significance thereto. The other kind of pigmentation, so well demonstrable by the Heidenhain method, is developed in all of our three cases. It is in this pigmentation, if in any feature now demonstrable, that we must look for somewhat differential characters in diseases of the group under discussion. The most significant feature of this type of pigmentation is its plurifocal distribution in the affected cells. Whereas the yellow sacks of the more banal type of pigmentation seem to enter into no intimate relation with the cell and may not interrupt its paths, the plurifocal pigmentation, on the contrary, is so distributed that it may well modify or influence the progress of impulses through the cells. It may be noted that this kind of pigment is apt to be deposited at the sides and inferior angles of the cells (*e. g.*, of the large pyramidal cells of the frontal cortex) and to neglect the perinuclear and apical portions of the cells.

If we take into account the iron-hematoxylin-staining pigment and leave out of account the banal yellow pigment, it appears that the larger elements (*e. g.*, Betz cells, solitary cells of Meynert) are not likely to be affected. The iron-hematoxylin-staining pigmentation proves to be maximal rather in those elements whose function we do not understand or term receptive. If this pigmentation can be taken as a sign of central disease, the disease appears to involve not so much the larger elements which come into immediate relation with the projection system as the smaller elements having to do with transference of impulses or having unknown functions.

General Summary and Remarks.

The disease group melancholia has a somewhat precarious footing in present-day psychiatry. The purest cases appear to occur in or about the climacteric era. The practical alienist is always reluctant to place a case in the group melancholia, lest it shortly transpire that the case should rather have been counted senile, or arteriosclerotic, or, in some other way, frankly organic. Moreover, it frequently appears that error may creep in the opposite direction and the patient, alleged to have melancholia, turn out to be actually a victim of some constitutional defect or of some acute psychosis.

We have found difficulty in resolving our ideas about the disease group melancholia and were for a time inclined to believe that any given case could perhaps be transmuted, as a matter of diagnosis, into some other group.

As a beginning in this group, we have here introduced three cases which, whether they fit any acknowledged grouping or not, appear to have certain features in common as well as certain instructive differences. The psychological color and, to some extent, the course of these cases recall some features of Cotard's syndrome.

In every case there were a few established instances of insanity in the direct line on one or other side. The hereditary features, interesting in each case, appear to have little in common, except the terminal continuous depressions in the mothers of two patients (cases II and III).

The lives of the three patients showed little which can be regarded as underlying their ultimate conditions. Case I used no alcohol, Case II drank beer with meals, Case III used alcohol moderately. Venereal history practically negative in all cases.

Occupations: clerk, I; mason, II; shoemaker, III.

Previous diseases: lumbago, I; pneumonia seven years before commitment, II; scarlet fever and purulent otitis media, æt. 3, and typhoid fever and la grippe with delirium, æt. 61, III.

Ages at onset: 48, I; (69) 75, II; 65, III.

Durations: 8 months, I; (8 years) 2 weeks, II; 24 ca. weeks, III.

Onset: gradual, I, III; sudden, II.

Assignable causes: financial worry, I; senility and domestic worry; nothing, æt. 65, III.

Physical conditions: arteriosclerosis in all cases; case III showed emaciation, nephritis, cystitis, increase of reflexes.

Mental states: ideas of negation in all cases, developing in case I after slowly increasing depression and agitation with delusions about self and family and questionable hallucinations; in case II, after gradual senile failure, as sudden deep depression with agitation, delusions of ruin of self and family, and suicidal attempt; and in case III, after slowly developing hypochondriacal depression.

The feelings of unreality and ideas of negation presented a certain variety in the three cases. Case I showed an alteration of personality, uttered frequently in such phrases as "I'm all gone, I'm dead to the world. I'm not G. E. H. I've made myself as Gibbs; I've been here as G. E. H." Case II showed a feeling of unreality, both as regards the outer world ("sunlight not real, sky not blue, people not real human beings") and as regards himself ("I can't move; I can't die"). Case III showed an alteration of point of view as to the outer world ("you're all great big men, and so strong; you must weigh over 400 pounds") and nihilistic ideas ("I am so small you can't see me; I've got no brains; and I can't talk; I've got no heart, and no stomach, and I can't swallow; I wouldn't burn if you throw me in the burning furnace").

The anatomical side of these cases presents several common aspects, but little which promises to explain the disease. Arteriosclerosis, when confined to the large branches of the circle of Willis, can scarcely be invoked as underlying symptoms of such specialized character as those under consideration.

Just as the patients showed strikingly little in alterations of reflexes (increase in case III), so the brains showed strikingly little in the shape of gross or focal alterations (small old cyst of softening in case II and mild chronic exudative process in case III).

Moreover, the brains gave little evidence of general or focal atrophy. No striking alterations in cortical topography and arrangement of layers could be detected on microscopic examination. Pigment-bearing cells in perivascular spaces were constantly found; and, in default of any suspicious localization of these, we must attribute them rather to the results of advancing years than to a special factor.

Neuroglia cell pigmentation was also quite constantly found; but this was not so universal in distribution as was the case with the perivascular cell pigmentation. Common to all three cases was a neuroglia cell pigmentation in the intermediate layers of the areas of cortex examined. The relation of the neuroglia cell pigmentation to cortical activity could not be made out. Satellite-cell pigmentation was not constant.

Nerve cell pigmentation was constantly found in the elements of moderate size in all parts of the cortex examined. This pigmentation was strikingly brought out by the use of iron hematoxylin. The pigmentation in question has a somewhat characteristic locus in the affected cells, fails to destroy their contours, and lies apparently in interstices in the cells. This interstitial nerve cell pigmentation, as brought out by iron hematoxylin, is to be sharply distinguished from the familiar yellow sack pigmentation of the major elements.

Pending the increase of knowledge concerning the pigments and fat-like deposits in general, we can at least investigate their occurrence topographically. It seems to us that, however fragmentary the present findings are and however far we may be from bringing such findings into relation with disorders of apperception, we have at least a promising field for investigating the conditions of what seems to be a truly cortical disorder. We are at present at work upon accessible cases of melancholia.